REMARKS

Rejection under 35 U.S.C. § 112, first and second paragraph

Reconsideration and withdrawal of rejection of claims 1,5,8 and 9 under 35 U.S.C. § 112 is respectfully requested.

Page two of the Office Action rejected claims 1, 5 and 8 under 35 U.S.C. § 112, first paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, and claims 1, 5 for failing to reasonably provide enablement.

Applicants respectfully traverse the rejection and request withdrawal of the rejection for the following reasons:

I. The Office has requested that the term "prodrug" be removed from the claims.

Claims 1, 5, and 8 have been amended to remove the term "prodrug." Therefore, Applicants request that the rejection be withdrawn.

II. The Office has rejected the term aryl as indefinite because "there are, in fact, multiple different definitions of aryl." The Office has also rejected the term heteroaryl as indefinite, citing In re Wiggins, 179 USPQ 421.

The Terms Aryl and Alkaryl are Definite

Applicants submit that the term aryl is defined on page 6, lines 30-31 of the specification, is well known in the art, and is definite. To satisfy definiteness, an applicant "need only reasonably apprise those skilled in the art of the scope of the invention." *Miles Laboratories v. Shandon, Inc.*, 27 USPQ2d 1123 (Fed. Cir. 1993). Determining whether a patent claim is definite requires analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification. The Office mentions that Judge Smith's footnote in the case *In re* Sus, 134 USPQ 301, mentions that there are multiple different definitions of aryl. In that case, however, there was no guidance in the specification regarding which definition was proper. However, in the present application, Applicants have provided guidance on page 6, lines 30-31. Likewise, Applicants have provided guidance for the term "aralkyl" on page 7, lines 3-5.

Therefore, Applicants have reasonably apprised those skilled in the art of the scope of the term aryl and aralkyl, and request that the rejection be withdrawn.

The Term Heteroaryl is Definite

Further, Applicants submit that the term 'heteroaryl' is distinguishable from the term 'heterocycle' cited in In re Wiggins, and is defininte. The Office cites to the case *In re* Wiggins, 179 USPQ 421, to support the rejection of the term "heteroaryl". The term at issue in *In re* Wiggins was "heterocycle. However, Applicants point out that the term at issue in this application is "heteroaryl," further defined in the claims as a "C_5-C_7 monocyclic heteroaryl ring." Therefore, the Wiggins case is inapposite to the term at issue in this application, and Applicants request that the rejection be withdrawn.

Objection under 37 CFR 1.141

I. The Office has objected to Claims 4 and 8 as failing to comply with 37 CFR 1.141, and as improper dependent claims.

Claims 4 and 8 are Not Ultimate Species Claims

The Office suggests that the species in claims 4 and 8 should be considered to be ultimate species, and not true dependent claims. Further, the Office points to the cost in searching as a reason for applying this policy. The Applicants respectfully point out that the cost associated with searching is not a criterion of patentability. Further, it is not correct that the Markush groups in claim 4 and 8 are ultimate species. Rather, each claim covers a group of compounds, properly classified as a genus. MPEP 809.02 states that under 37 CFR 1.141, an allowed generic claim may link a reasonable number of species embraced thereby.

The Office's argument also raises the specter of *In re* Webber, 198 USPQ 328, which rejected the restriction practice under 121 was applied to restrict each species into a separate application. In his concurrence, Judge Rich stated that "It is elementary patent law that the number of 'species' 'covered' by a patent having a generic claim is virtually without limit notwithstanding the limitation of Rule 141 to five species "specifically claimed." So the discretionary power to limit one application to one

invention is no excuse at all for refusing to examine a broad generic claim -- no matter how broad, which means no matter how many independently patentable inventions may fall within it."

Further, this same rejection was given in the application at issue in United Sweetener USA, Inc. v. The Nutrasweet Company, 19 USPQ 2D 1561. The PTO objected to claims 2-6, stating that "they were in fact ultimate species and thus [did] not qualify as true dependent claims." However, the CAFC stated that "Nutrasweet requested that the objection to claims 2 through 6 be rescinded in light of a recent administrative ruling from the PTO." Therefore, this issue was decided in an administrative ruling between the O.G. notice cited by the Office in this application and December 6, 1968, when Nutrasweet responded to the same rejection.

Forcing the Applicant to One Species Per Claim Does Not Satisfy the Requirements of 37 CFR 1.141(a).

The Rule in 37 CFR 1.141(a) states that:

Two or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependant form or otherwise include all the limitations of the generic term.

There is little guidance on what a reasonable number would be, but Applicants believe that the term "reasonable number" was broadening the number allowable under the original 1.141 from 5. Therefore, forcing Applicants to one species is not reasonable under the amended 1.141. Further, in several issued patents, including, for example, US Patent 6,376,503, Claim 11, uses similar Markush language as in the present application, and lists 23 compounds. Therefore, Applicants point out that Claims 4 and 8 each claim a reasonable number of species.

Rejection under 35 U.S.C. § 101, Restriction under MPEP 806.05(h)

I. The Examiner has asserted that Claim 9 "does not relate to the real world of commerce". Further, the Examiner has asserted that "[t]he Board of Appeals and the C.C.P.A. have held that even though the specification does not mention human use specifically, the Patent Office is not precluded from finding an inference of human use and require proof thereof, when such use is a medical nature for the treatment of a serious disease."

II. The Office has removed claims 9-18 from consideration under MPEP 806.05(h).

Inhibition of the Alpha-v Beta-3 Integrin is a Real World Utility

Applicants assert that inhibition of the alpha-v beta-3 integrin is a real world utility. MPEP 2107 contrasts the situation where an applicant merely indicates that a compound may be useful in treating unspecified disorders with "the situation where applicant discloses a specific biological activity" (in this instance, the inhibition of the alphav-beta3 integrin) "and reasonably correlates that activity to a disease condition" (in this instance, the specification on page 6, lines 1-14, provides that inhibition of avb3 will be useful in treating a variety of conditions or disease states including tumor metastasis, solid tumor growth (neoplasia), osteoporosis, Paget's disease, humoral hypercalcemia of malignancy, angiogenesis, including tumor angiogenesis, retinopathy, including macular degeneration, arthritis, including rheumatoid arthritis, periodontal disease, psoriasis and smooth muscle migration (e.g., restenosis arhterosclerosis), viral infection, fungal infection, and other microbial infection). Literature supporting the correlation between the avb3 integrin and these disease states was provided in the specification on pages 2-4. Therefore, applicants have provided a specific, credible real world utility for Claim 9.

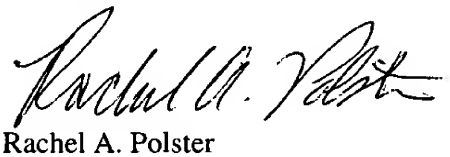
Claims 9-18 Were Improperly Removed from Consideration

MPEP 806.05(h) states that "A product an a process of using the product can be shown to be distinct inventions if either or both of the following can be shown: (A) the process of using as claimed can be practiced

with another materially different product, or (B) the product as claimed can be used in a materially different process." Applicants maintain that the restriction out of claims 9-18 was improper. No restriction requirement was received, nor an election made by applicants. Applicants request a proper restriction requirement describing the inventions the Office considers distinct.

In view of the foregoing remarks, it is submitted that all claims now active in the present application are in condition for allowance. Therefore, passage of the application and claims to issue is requested.

Respectfully submitted,



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St. Louis, MO 63167

PATENT Case S00328 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

Vianello et al. | GROUP ART UNIT: 1624

SERIAL NUMBER: 09/924,732 | EXAMINER: J. Ford

FILED: August 8, 2001 | DATE: December 5, 2002

TITLE: NEW BENZOXAZINE DERIVATIVES USEFUL AS INTEGRIN RECEPTOR ANTAGONISTS

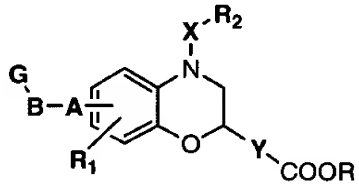
I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington D.C., 20231 on December 5, 2002
Rachel A. Polster

Rachel A. Polster Date: December 5, 2002

APPENDIX TO AMENDMENT

Version of Claims with Markings to Show Changes Made

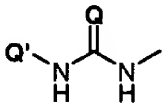
1. (once amended) A compound of the formula (I)



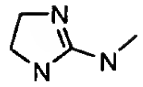
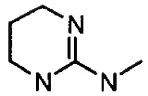
(I)

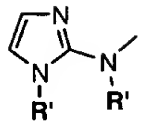
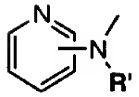
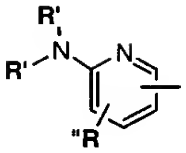
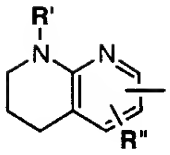
or a pharmaceutically acceptable salt[, prodrug] or ester thereof, wherein:

G is selected from the group consisting of

a) 

wherein Q is NH or O and Q' is selected from the group consisting of H, C_1-C_6 alkyl, phenyl, and phenyl-C_1-C_4-alkyl;

b)  c) 

d)  e)  f)  g) 

wherein **R'** and **R''** are independently H or C_1-C_4-alkyl;

B is C_1-C_4 alkyl or C_2-C_4 alkenyl;

A is selected from the group consisting of CH_2, O, $S(O)_p$ wherein p is zero, 1 or 2, NH, a group CON(R''') or N(R''')CO wherein R''' is hydrogen or CH_3;

R_1 is selected from the group consisting of H, C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, halogen, and CF_3;

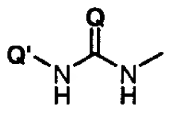
X is $(C=O)_m$ wherein m is 0 or 1 ;

R_2 is selected from the group consisting of H, C_1-C_4 alkyl, C_3-C_7 cycloalkyl, C_1-C_4-alkylcycloalkyl; aryl unsubstituted or optionally substituted by one to three substituents independently selected from halogen, CF_3, C_1-C_4 alkyl, hydroxy and C_1-C_4 alkoxy; aralkyl; and C_5-C_7 monocyclic heteroaryl ring containing one to three heteroatoms selected from O, S, and N, unsubstituted or optionally substituted by one to three substituents independently selected from the group consisting of halogen, CF_3, C_1-C_4 alkyl, hydroxy and C_1-C_4 alkoxy;

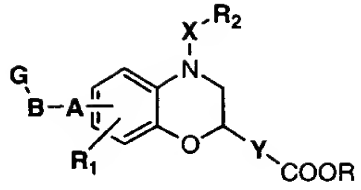
Y is $(CH_2)_n$ wherein n is 1 or 2;

R is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, aryl or aryl-C_1-C_4 alkyl.

With the proviso that m can not be 0 when G is :

a)  wherein Q' is H and Q is O and X is $(C=O)_m$.

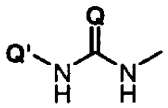
5. (once amended) A pharmaceutical composition comprising a therapeutically effective amount of the compound of the formula (I):



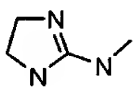
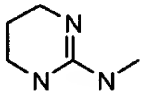
(I)

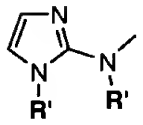
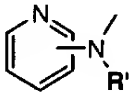
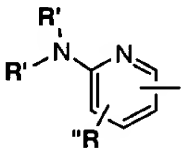
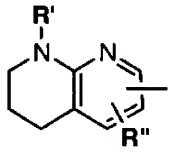
or a pharmaceutically acceptable salt[, prodrug] or ester thereof, wherein:

G is selected from the group consisting of

a) 

wherein Q is NH or O and Q' is selected from the group consisting of H, C_1-C_6 alkyl, phenyl, and phenyl-C_1-C_4-alkyl;

b)  c) 

d)  e)  f)  g) 

wherein **R'** and **R''** are independently H or C_1-C_4-alkyl;

B is C_1-C_4 alkyl or C_2-C_4 alkenyl;

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R_1 is selected from the group consisting of H, C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, halogen, and CF_3;

X is $(C=O)_m$ wherein m is 0 or 1 ;

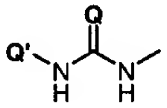
R_2 is selected from the group consisting of H, C_1-C_4 alkyl, C_3-C_7 cycloalkyl, C_1-C_4-alkylcycloalkyl; aryl unsubstituted or optionally substituted by one to three substituents independently selected from halogen, CF_3, C_1-C_4 alkyl, hydroxy and C_1-C_4 alkoxy; aralkyl; and C_5-C_7 monocyclic heteroaryl ring containing one to three heteroatoms selected from O, S, and N, unsubstituted or optionally substituted by one to three substituents independently selected from the group consisting of halogen, CF_3, C_1-C_4 alkyl, hydroxy and C_1-C_4

alkoxy;

Y is $(CH_2)_n$ wherein n is 1 or 2;

R is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, aryl or aryl-C_1-C_4 alkyl.

With the proviso that m can not be 0 when G is :

a)  wherein Q' is H and Q is O and X is $(C=O)_m$.